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By _____
(Signature of person mailing)
Tracy Mycroft
(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: **Aubrecht, et al.**

SERIAL NO.: **10/029,741** EXAMINER: **Wessendorf, T.D.**

FILED: **12/21/2001** ART UNIT: **1639**

FOR: **Novel Bioluminescent Assay and Bacterial Strains Useful Therein**

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

RESPONSE UNDER 37 CFR §1.111

Applicants hereby respond to the Final Office Action mailed November 17, 2003 in the subject patent application.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 8-15 as failing to comply with the written description requirement for failing to provide a description of a histidine gene or a tryptophan gene.

The Examiner supports the rejection with the statement that "the description in the original specification relates to his or trp as a point mutation in the gene and not what appears as the claimed gene itself."

The U.S. Court of Appeals for the Federal Circuit has explained that the purpose of the written description requirement is to assure that the inventor was in possession of the claimed invention as of the filing date of his patent. *See Lockwood v. American Airlines, Inc.*, 107 F.3d at 1565, 1572, 41 U.S.P.Q. 2d. 1961, 1966 (Fed. Cir. 1997).

Applicants submit that claims 9 and 11 have been misconstrued by the Examiner: that claim 9 claims a histidine gene and claim 11 claims a tryptophan gene. In fact, Claim 9 does not claim a histidine gene, but rather, a cell having, *inter alia*, a reversible point mutation in a histidine gene. Likewise, claim 11 does not claim a tryptophan gene, but rather, a cell having, *inter alia*, a reversible point mutation in a tryptophan gene.

As stated by the Examiner, the specification describes a point mutation in the *his* or *trp* genes. Hence, the claims comply with the written description requirement.

Based upon the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 8-15 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Examiner bases the rejection on two points: first, that it is not clear whether a "reversible point mutation of a gene" is different from the gene complex or a part of the gene complex; and, second, that claim 9 is unclear as to how "histidine" is considered a gene, with similar import to claim 11.

In order to determine whether the statutory requirement of having claims that particularly point out and distinctly claim the subject matter of the invention has been met requires a determination whether those skilled in the art would understand what is claimed. *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), cert. denied, 502 U.S. 856 (1991).

With regard to the Examiner's first point as to the distinction between "reversible point mutation of a gene" and a gene complex, Applicants point out that none of claims 8-15 recite a "gene complex" per se, but rather a *lux(CDABE)* gene complex. Applicants maintain that one skilled in the art would clearly understand the meaning of each of the terms, "*lux(CDABE)* gene complex" and "reversible point mutation of a gene", and, as such, would be able to distinguish between the two.

Applicants have explicitly defined the term "point mutation" as a mutation that causes the replacement of a single base pair with another base pair (*see* Specification, page 12, lines 20-21). The term "mutation" is likewise defined as a change in the DNA

sequence of an organism due to, e.g., gene or point mutations, primary DNA damage and repair, or chromosomal alterations (*see* Specification, page 1, lines 13-15). Both of these definitions are essentially the same as those in The Dictionary of Cell & Molecular Biology, 3rd Edition, by Lackie, J.M and Dow, J.A.T., published in 1999 by Academic Press (New York), cited by Applicants in the Specification on page 11, lines 21-22. In turn, the meaning of the term "reversible point mutation of a gene" would be understood by those with skill in the art, especially in the context of the Specification description and claims (*see, for example,* Specification, page 6, lines 29-30, page 7, lines 3-4 and page 7, lines 11-12.

The term "*lux(CDABE)* gene complex" would be well understood by those with skill in the art, especially in the context of the Specification description and claims. *Lux(CDABE)* gene complex is understood to mean the *Lux* operon as described in detail in the Specification. *See, for example*, Specification, page 4, lines 5-22 and page 8, line 10.

With regard to the Examiner's second point that in claim 9 it is unclear as to how histidine is considered a gene, Applicants submit that, again, the term "histidine gene" would be understood by those with skill in the art, especially in the context of the Specification description and claims. In describing bacterial mutants used in the Ames Assay, the Specification provides, "these mutants each have a unique reversible point mutation in one of the histidine genes which renders them incapable of producing histidine." (Specification, page 15, lines 4-5). The histidine genes having such mutations, and cells incorporating such mutations, are well known in the art as illustrated in the Specification with reference to Ames, B.N. et al., Methods for detecting carcinogens and mutagens with *Salmonella*/mammalian-microsome mutagenicity test," *Mutation Res.* 31: 347-364 (1975) (*see* Specification, page 19, line 23 to page 20, line 2.

The Examiner's second point seems directed, also, to the term "tryptophan gene" in claim 11. Again, Applicants submit that the term "tryptophan gene" would be understood by those with skill in the art, especially in the context of the Specification description and claims. For example, as with "histidine gene", "tryptophan gene" is relevant in the context of a point mutation contained therein. The tryptophan genes having such mutations, and cells incorporating such mutations, are well known in the

art as illustrated in the Specification. *See* Specification, page 3, lines 27-30 and page 20, lines 3-16.

Based upon the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection of Claims Under 35 U.S.C. § 102

The Examiner has maintained her rejection of claims 8-10 and 12-15 under 35 U.S.C. § 102(b) as being anticipated by WO 94/13831 (Larossa et al.). Applicants respectfully maintain their traversal of the rejection and ask the Examiner to consider the following points:

Applicants claim cells comprising an expressible gene complex and a reversible point mutation of a gene.

Larossa does not disclose any cell having both an expressible gene complex and a reversible point mutation of a gene. As stated by the Examiner in the last Office Action, "Larossa discloses said cell comprising a lux gene with his gene". Even if correct, Larossa does not describe a cell with a reversible point mutation on the *his* gene.

With respect to the reference in Larossa to the use of serine hydroxamate, the Examiner appears to have confused the recitation in claim 14 of a point mutation at a codon for a serine amino acid on β-lactamase with the use by Larossa of a reagent – serine hydroxamate – that happens to contain the word "serine". Furthermore, the Examiner's statement that Applicants must now show that serine hydroxamate does not cause mutations in the gene has no basis in law. Notwithstanding, serine hydroxamate is described as an inhibitor of seryl-tRNA synthase which inhibits protein synthesis (*See* Larossa at page 59, line 13-16; Pizer and Tosa (1971), *J. Bacteriol.*, 106, 972-982 at page 972 (enclosed herewith)) and bears no relation to a point mutation in a serine codon.

Based upon the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection of Claims Under 35 U.S.C. § 103

The Examiner has maintained her rejection of claims 11 under 35 U.S.C. §103(a) as being anticipated by WO 94/13831 (Larossa et al.) in view of Green et al (1976). Applicants again respectfully traverse the rejection. For the reasons submitted above regarding the rejection under §102, Applicants again submit that Larossa does not disclose the bacterial strains claimed by Applicants having mutations on *his* or *ser.* As made clear by the Examiner in her first Office Action dated January 6, 2003, Green merely describes *E. coli* having a *trp* mutation. Therefore, it is not possible that one skilled in the art would be motivated to combine Larossa with Green to reach Applicants' invention.

Based upon the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Based on the foregoing, it is believed that the application is in condition for allowance. Such prompt and favorable action is requested.

Respectfully submitted,

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